

Appendix C

1. An immunological composition comprising:

a physiologically acceptable non-toxic vehicle containing a purified non-proteolytic cysteine protease, which produces an immune response in a mammal against Group A streptococcal infection, wherein said cysteine protease comprises at least one amino acid substitution and said amino acid substitution occurs at the amino acid position selected from the group consisting of Lys145, Gln185, Cys192, His340, Asn356 and Trp357.
4. The immunological composition of claim 1, wherein said infection is selected from the group consisting of pharyngitis, tonsillitis, skin infections, acute rheumatic fever, scarlet fever, post-streptococcal glomerulonephritis, and toxic-shock-like syndrome.
5. The immunological composition of claim 1 further comprising a purified streptococcal M protein antigen.
6. A method of producing an immune response in mammals comprising:

administering to a mammal an immunological composition comprising, a purified non-proteolytic cysteine in an amount sufficient to produce an immune response to a Group A streptococcal infection, wherein said cysteine protease comprises at least one amino acid substitution and said amino acid substitution occurs at the amino acid position selected from the group consisting of Lys145, Gln185, Cys192, His340, Asn356 and Trp357.
7. The method of claim 6, wherein said immunological composition is given by parenteral administration.
8. The method of claim 7, wherein said parenteral administration is selected from the group consisting of subcutaneous administration and intramuscular administration.

9. The method of claim 6, wherein said immunological composition is administered orally.
10. The method of claim 6, wherein said infection is selected from the group consisting of pharyngitis, tonsillitis, skin infections, acute rheumatic fever, scarlet fever, post-streptococcal glomerulonephritis, sepsis, and toxic-shock-like syndrome.
11. The method of claim 6, wherein said immunological composition is administered in multiple doses.
12. The method of claim 6 further comprising:
administering to the mammal a purified streptococcal M protein antigen.
13. The method of claim 12, wherein said immunological composition is given by parenteral administration.
14. The method of claim 13, wherein said parenteral administration is selected from the group consisting of subcutaneous administration and intramuscular administration.
15. The method of claim 12, wherein said immunological composition is administered orally.
16. The method of claim 12, wherein said infection is selected from the group consisting of pharyngitis, tonsillitis, skin infections, acute rheumatic fever, scarlet fever, post-streptococcal glomerulonephritis, sepsis, and toxic-shock-like syndrome.
17. The method of claim 12, wherein said immunological composition is administered in multiple doses.
18. The immunological composition of claim 1, where said mammal is human.
19. The method of claim 6, wherein said mammal is a human.

20. The immunological composition of claim 1, wherein said amino acid substitution is selected from the group consisting of Lys145→Ala145, Cys192→Ala192, Cys192→Ser192, His340→Ala340, Gln185→Ala185, Asn356→Ala356 and Trp357→Ala357.
21. The method of claim 6, wherein said amino acid substitution is selected from the group consisting of Lys145→Ala145, Cys192→Ala192, Cys192→Ser192, His340→Ala340, Gln185→Ala185, Asn356→Ala356 and Trp357→Ala357.
22. The immunological composition of claim 20, wherein said amino acid substitution is Cys192→Ala192 or Cys192→Ser192.
23. The method of claim 21, wherein the amino acid substitution is Cys192→Ala192 or Cys192→Ser192.
24. The immunological composition of claim 1, wherein said amino acid substitution occurs at Lys145.
25. The immunological composition of claim 1, wherein said amino acid substitution occurs at Cys192.
26. The immunological composition of claim 1, wherein said amino acid substitution occurs at Gln185.
27. The immunological composition of claim 1, wherein said amino acid substitution occurs at Asn356.
28. The immunological composition of claim 1, wherein said amino acid substitution occurs at Trp357.
29. The immunological composition of claim 1, wherein said amino acid substitution occurs at His340.
30. The method of claim 6, wherein said amino acid substitution occurs at Lys145.

31. The method of claim 6, wherein said amino acid substitution occurs at Cys192.
32. The method of claim 6, wherein said amino acid substitution occurs at His340.
33. The method of claim 6, wherein said amino acid substitution occurs at Gln185.
34. The method of claim 6, wherein said amino acid substitution occurs at Asn356.
35. The method of claim 6, wherein said amino acid substitution occurs at Trp357.
45. An immunological composition comprising a purified non-proteolytic cysteine protease, which produces an immune response to a mammal against Group A streptococcal infection, wherein said cysteine protease comprises at least one amino acid substitution and said amino acid substitution occurs at the amino acid position selected from the group consisting of Lys145, Gln185, Cys192, His340, Asn356 and Trp357.
46. A method of producing an immune response in mammals comprising:

administering to a mammal the immunological composition of claims 1,5, 20, 22, 24, 25, 26, 27, 28, 29, or 44 in an amount sufficient to produce an immune response to a Group A streptococcal infection.
47. The method of claim 45, the mammal is human.